Biomarker DB Prototype Requirements

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This is a draft version intended to stimulate discussion to develop a Biomarker DB prototype. Please feel free to contact me with suggestions, comments, or questions.

Table of Contents

1. Introduction

This is a draft Biomarker DB prototype requirements document. This document includes three data models which represent three different types of biomarker studies as follows:

- Section 2.1 shows a data model of biomarker data which could be populated from "**scientific**" type publications. "**Scientific**" type publications are for authors to report their own tumor marker discovery and validation studies as well as clinical trial studies and to highlight areas and approaches that appear most promising for early detection of cancer.

- Section 3.1 shows a data model of biomarker data which could be collected from "**review**" type publications. "**Review**" type publications are for authors to compare and provide an overview of the large number of other people's studies that have correlated to a variety of markers.

- Section 4.1 shows a data model of biomarker data which could be populated from "**technology**" type publications. "**Technology**" type publications are for authors to report their experiences with new technology (e.g., SELDI-TOF-MS) and to provide their evaluations on the technology.

Using these three data models, biomarker data were populated from the following three publications:

- Section 2.2 shows biomarker data populated from a "**scientific**" type publication, "Phillips M, Cataneo RN, Cummin AR, Gagliardi AJ, Gleeson K, Greenberg J, Maxfield RA, Rom WN. Detection of lung cancer with volatile markers in the breath. Chest. 2003 Jun;123(6):2115-23. PMID: 12796197."

- Section 3.2 shows biomarker data populated from a "**review**" type publication, "Perkins GL, Slater ED, Sanders GK, Prichard JG. Serum tumor markers. Am Fam Physician. 2003 Sep 15;68(6):1075-82. PMID: 14524394."

- Section 4.2 shows biomarker data populated from a "**technology**" type publication, "Liu AY, Zhang H, Sorensen CM, Diamond DL. Analysis of prostate cancer by proteomics using tissue specimens. J Urol. 2005 Jan;173(1):73-8. Erratum in: J Urol. 2005 Mar;173(3):1051. PMID: 15592032."

In addition, the document includes two examples of query:

- Section 2.3 shows an example query and the prototype system may allow users to do the followings:
  - asking for all markers listed in rank order according to sensitivity or specificity, etc.
  - for being able to make such queries about samples - cancer type, cancer stage 1 or 2, age 50-55, non-smoker.

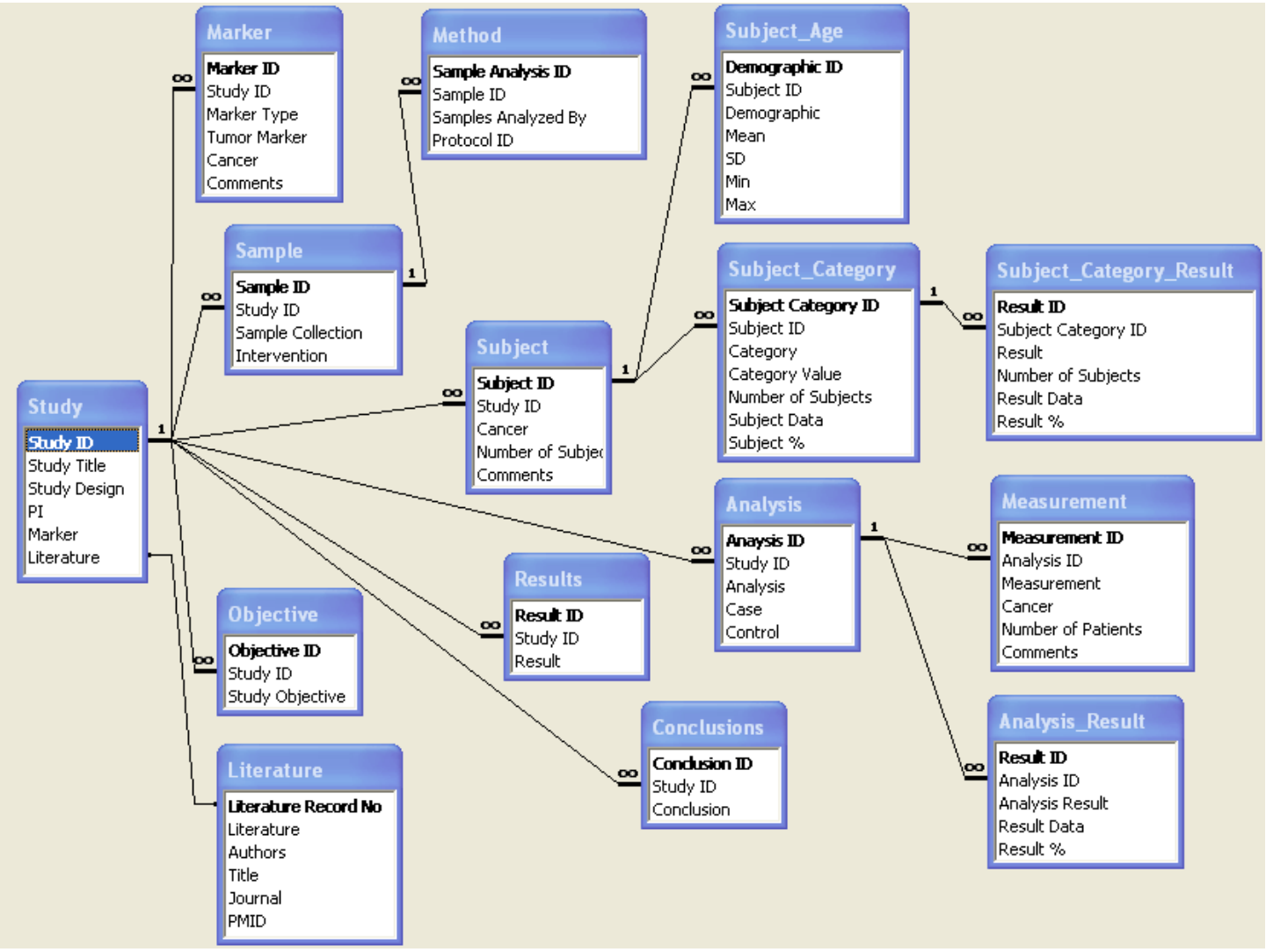
- Section 3.3 shows an example query and the prototype system may allow users to do the followings:
  - asking for all markers listed in rank order according to sensitivity or specificity, etc.
  - for being able to make such queries about comparative data of the large number of studies.

Finally, the document includes two examples of science data that might be available in eCAS system and link to the Biomarker DB:

- Section 4.3 shows two basic types of science data for proteomics studies such as tissue staining (Immunohistochemistry, IHC) and microarray (MA, using Affymetrix human chips) expression analysis. Sections 4.3.1, 4.3.2, and 4.3.2 shows the Systems Biology Institute's database schema to capture data of staining (Immunostain.gif) and microarray (Microarray_Affy_Schema.gif) and the xml file (ms_data_1.tar).

2. Biomarker data populated from "scientific" type publications

2.1 Data Model



2.2 Data

Study					
Study ID	**Study Title**	**Study Design**	**PI**	**Marker**	**Literature**
1	Detection of lung cancer with volatile markers in the breath.	Combined case-control and cross-sectional study	William Rom	Butane; Tridecane, 3-methyl; Tridecane, 7-methyl; Octane, 4-methyl; Hexane, 3-methyl; Heptane; Hexane, 2-methyl; Pentane; Decane, 5-methyl.	1

Literature

Literature Record No	Literature	Authors	Title	Journal	PMID
1	Phillips M, Cataneo RN, Cummin AR, Gagliardi AJ, Gleeson K, Greenberg J, Maxfield RA, Rom WN. Detection of lung cancer with volatile markers in the breath. Chest. 2003 Jun;123(6): 2115-23.	Phillips M, Cataneo RN, Cummin AR, Gagliardi AJ, Gleeson K, Greenberg J, Maxfield RA, Rom WN.	Detection of lung cancer with volatile markers in the breath.	Chest. 2003 Jun; 123(6):2115-23.	12796197

Objective

Objective ID	Study ID	Study Objective
1	1	To evaluate volatile organic compounds in the breath as tumor markers in lung cancer.
2	1	Alkanes and monomethylated alkanes are oxidative stress products that are excreted in the breath, the catabolism of which may be accelerated by polymorphic cytochrome p450-mixed oxidase enzymes that are induced in patients with lung cancer.

Marker

Marker ID	Study ID	Marker Type	Tumor Marker	Cancer	Comments
1	1	Volatile organic compound	Butane; Tridecane, 3-methyl; Tridecane, 7-methyl; Octane, 4-methyl; Hexane, 3-methyl; Heptane; Hexane, 2-methyl; Pentane; Decane, 5-methyl.	Lung cancer	Butane is the best single discriminator.

Study_Results

Result ID	Study ID	Result
1	1	???

Conclusion

Conclusion ID	Study ID	Conclusion
1	1	Bronchoscopy and biopsy

Sample

Sample ID	Study ID	Sample Collection	Intervention
1	1	Breath collection	Breath samples were analyzed by gas chromatography and mass spectroscopy to determine alveolar gradients (ie, the abundance in breath minus the abundance in room air) of C4-C20 alkanes and monomethylated alkanes.

Method

Sample Analysis ID	Sample ID	Samples Analyzed By	Protocol ID
1	1	Gas chromatography	
2	1	Mass spectroscopy	

Subject

Subject ID	Study ID	Cancer	Number of Subjects	Comments
1	1	Bronchoscopy negative for cancer	91	

Subject				
2	1	Primary lung cancer	67	10 small cell and 57 non-small cell cancers.
3	1	Metastatic lung cancer	15	
4	1	Lung cancer, undetermined	5	Lung cancer was classified as undetermined when it was not possible to determine with certainty whether it was metastatic to the lung or it had arisen as a lung primary (eg, an adenocarcinoma of indeterminate primary origin).
5	1	Healthy volunteers	41	

Subject_Age						
Demographic ID	Subject ID	Demographic	Mean	SD	Min	Max
1	1	Age, yr	58.4	14.2		
2	2	Age, yr	68.2	9.9		
3	3	Age, yr	66.6	9.2		
4	4	Age, yr	63.0	28.3		
5	5	Age, yr	69.6	12.6		

Subject_Category						
Subject Category ID	Subject ID	Category	Category Value	Number of Subjects	Subject Data	Subject %
1	1	Gender	Male	48	48/67	71.6
2	1	Gender	Female	19	19/67	28.4
3	1	Gender	Total	67		
4	2	Gender	Male	41	41/91	45.1
5	2	Gender	Female	50	50/91	54.9
6	2	Gender	Total	91		
7	3	Gender	Male	4	4/15	26.7
8	3	Gender	Female	11	11/15	73.3
9	3	Gender	Total	15		
10	4	Gender	Male	3	3/5	60.0
11	4	Gender	Female	2	2/5	40.0
12	4	Gender	Total	5		
13	5	Gender	Male	16	16/41	39.0
14	5	Gender	Female	25	25/41	61.0
15	5	Gender	Total	41		
16	1	Smoking status	Smokers and ex-smokers	64		
17	1	Smoking status	Nonsmokers	3		
18	1	Smoking status	Total	67		
19	1	Histology	Non-small cell cancer	57		
20	1	Histology	Small cell cancer	10		
21	1	Histology	Total	67		
22	1	TNM staging	Stage 1	14		

Subject_Category						
23	1	TNM staging	Stage 2	2		
24	1	TNM staging	Stage 3	20		
25	1	TNM staging	Stage 4	23		
26	1	TNM staging	Total	59		
27	5	Smoking status	Smokers and ex-smokers	23		
28	5	Smoking status	Nonsmokers	18		
29	5	Smoking status	Total	41		

Subject_Category_Result					
Result ID	Subject Category ID	Result	Number of Subjects	Result Data	Result %
1	16	Sensitivity	55	55/64	85.9
2	17	Sensitivity	2	2/3	66.7
3	18	Sensitivity	57	57/67	85.1
4	19	Sensitivity	50	50/57	87.8
5	20	Sensitivity	7	7/10	70.0
6	21	Sensitivity	57	57/67	85.1
7	22	Sensitivity	12	6/7	85.7
8	23	Sensitivity	1	1/2	50.0
9	24	Sensitivity	18	9/10	90.0
10	25	Sensitivity	19	19/23	82.6
11	26	Sensitivity	50	50/59	84.7
12	27	Specificity	19	19/23	82.6
13	28	Specificity	14	7/9	77.8
14	29	Specificity	33	33/41	80.5

Analysis				
Anaysis ID	Study ID	Analysis	Case	Control
1	1	A predictive model was constructed using forward stepwise discriminant analysis of the alveolar gradients.	Patients with primary lung cancer	Healthy volunteers
2	1	Cross-validation using leave-one-out jackknife technique.	Patients with primary lung cancer	Healthy volunteers
3	1	Cross-validation in patients with metastatic lung cancer (sensitivity check).	Patients with metastatic lung cancer	
4	1	Cross-validation in patients with negative biopsies (specificity check).		Patients with negative biopsies
5	1	Lung cancer screening with the breath test.	Lung cancer	No cancer

Measurement					
Measurement ID	Analysis ID	Measurement	Cancer	Number of Patients	Comments
1	1	Positive test result	Primary lung cancer patients	60	TP
2	1	Negative test result	Primary lung cancer patients	7	FN
3	1	Positive test result	Healthy volunteers	34	FP
4	1	Negative test result	Healthy volunteers	7	TN

Measurement					
5	2	Positive test result	Primary lung cancer patients	57	TP
6	2	Negative test result	Primary lung cancer patients	10	FN
7	2	Positive test result	Healthy volunteers	33	FP
8	2	Negative test result	Healthy volunteers	8	TN
9	3	Positive test result	Metastatic lung cancer patients	10	TP
10	3	Negative test result	Metastatic lung cancer patients	5	FN
11	4	Positive test result	No cancer patients	34	FP
12	4	Negative test result	No cancer patients	15	TN
13	5	Positive test result	Lung cancer	23	TP
14	5	Negative test result	Lung cancer	4	FN
15	5	Positive test result	No cancer	190	FP
16	5	Negative test result	No cancer	783	TN

Analysis_Result				
Result ID	Analysis ID	Analysis Result	Result Data	Result %
1	1	Sensitivity	60/67	89.6
2	1	Specificity	34/41	82.9
3	2	Sensitivity	57/67	85.1
4	2	Specificity	33/41	80.5
5	3	Sensitivity	2/3	66.7
6	4	Specificity	34/49	37.4
7	5	Sensitivity	23/27	85.1
8	5	Specificity	783/973	80.5
9	5	PPV	23/213	10.8
10	5	NPV	783/787	99.5

2.3 Query

Study Title	**Detection of lung cancer with volatile markers in the breath.**
PI	**William Rom**
Study Design	**Combined case-control and cross-sectional study**
Marker	**Butane; Tridecane, 3-methyl; Tridecane, 7-methyl; Octane, 4-methyl; Hexane, 3-methyl; Heptane; Hexane, 2-methyl; Pentane; Decane, 5-methyl.**

Analysis A predictive model was constructed using forward stepwise discriminant analysis of the alveolar gradients.
Case Patients with primary lung cancer
Control Healthy volunteers

Analysis Result	Result Data	Result %
Specificity	34/41	82.9
Sensitivity	60/67	89.6

Analysis Cross-validation using leave-one-out jackknife technique.
Case Patients with primary lung cancer
Control Healthy volunteers

Analysis Result	Result Data	Result %
Specificity	33/41	80.5
Sensitivity	57/67	85.1

Analysis Cross-validation in patients with metastatic lung cancer (sensitivity check).
Case Patients with metastatic lung cancer
Control

Analysis Result	Result Data	Result %
Sensitivity	10/15	66.7

Analysis Cross-validation in patients with negative biopsies (specificity check).
Case
Control Patients with negative biopsies

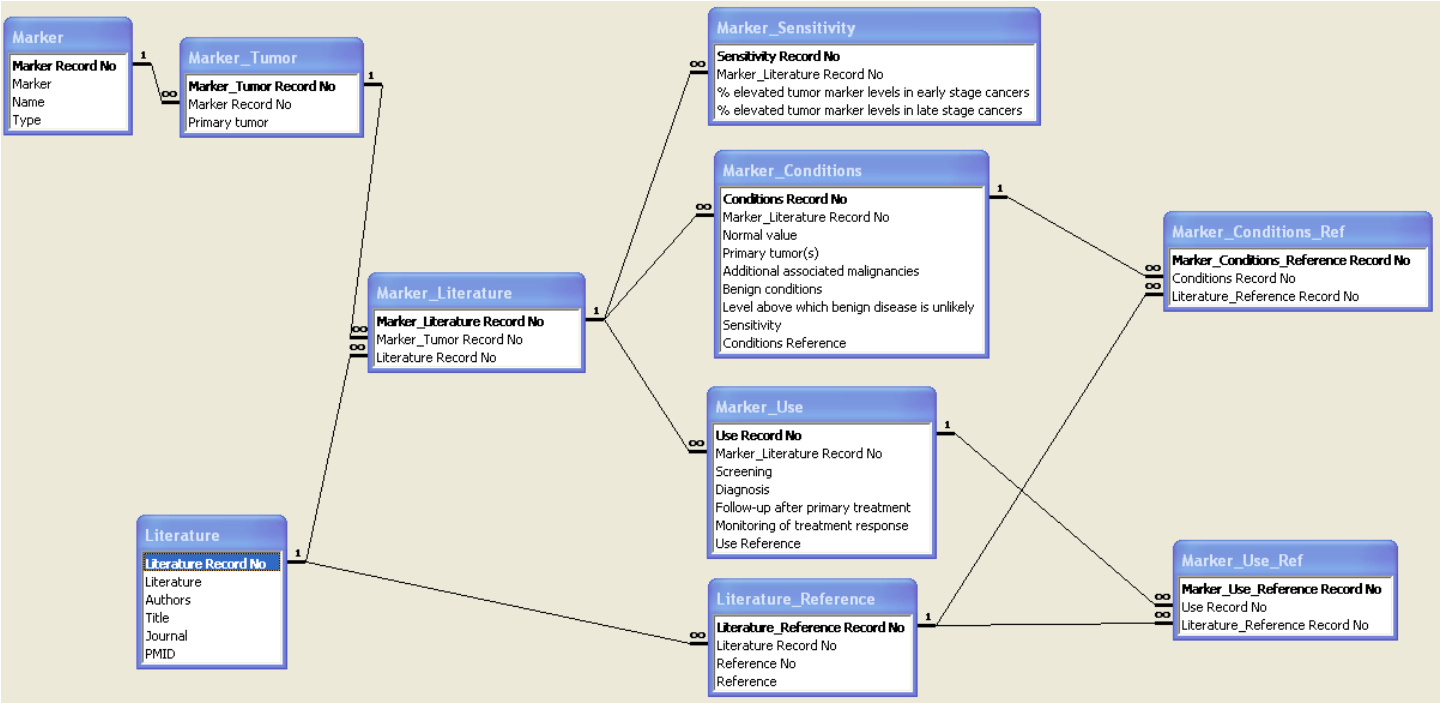
Analysis Result	Result Data	Result %
Specificity	34/49	37.4

Analysis Lung cancer screening with the breath test.
Case Lung cancer
Control No cancer

Analysis Result	Result Data	Result %
NPV	783/787	99.5
PPV	23/213	10.8
Specificity	783/973	80.5
Sensitivity	23/27	85.1

3. Biomarker data collected from “review” type publications

3.1 Data Model



3.2 Data

Marker			
Marker Record No	**Marker**	**Name**	**Type**
1	CA 27.29	cancer antigen 27.29	Serum
2	CEA	carcinoembryonic antigen	Serum
3	CA 19-9	cancer antigen 19-9	Serum
4	AFP	alpha-fetoprotein	Serum
5	b-hCG	beta subunit of human chorionic gonadotropin	Serum
6	CA 125	cancer antigen 125	Serum
7	PSA	prostate-specific antigen	Serum

Marker_Tumor		
Marker_Tumor Record No	**Marker Record No**	**Primary tumor**
1	1	Breast cancer
2	2	Colorectal cancer
3	3	Pancreatic cancer
4	3	Biliary tract cancer
5	4	Hepatocellular carcinoma
6	4	Nonseminomatous germ cell tumor
7	5	Nonseminomatous germ cell tumor
8	5	Gestational trophoblastic disease

Marker_Tumor

9	6	Ovarian cancer
10	7	Prostate cancer

Literature

Literature Record No	Literature	Authors	Title	Journal	PMID
1	Perkins GL, Slater ED, Sanders GK, Prichard JG. Serum tumor markers. Am Fam Physician. 2003 Sep 15;68(6): 1075-82.	Perkins GL, Slater ED, Sanders GK, Prichard JG.	Serum tumor markers.	Am Fam Physician. 2003 Sep 15;68(6): 1075-82.	14524394

Marker_Literature

Marker_Literature Record No	Marker_Tumor Record No	Literature Record No
1	1	1
2	2	1
3	3	1
4	4	1
5	5	1
6	6	1
7	7	1
8	8	1
9	9	1
10	10	1

Marker_Sensitivity

Sensitivity Record No	Marker_Literature Record No	% elevated tumor marker levels in early stage cancers	% elevated tumor marker levels in late stage cancers
1	1	33	67
2	2	25	75
3	3	80	90
4	4	60	70
5	5	80	80
6	6	20	85
7	7	20	85
8	8	?	?
9	9	50	85
10	10	75	75

Marker_Conditions

Conditions Record No	Marker Literature Record No	Normal value	Primary tumor(s)	Additional associated malignancies	Benign conditions	Level above which benign disease is unlikely	Sensitivity	Conditions Reference

Marker_Conditions								
1	1		Breast cancer	Colon, gastric, hepatic, lung, pancreatic, ovarian, and prostate cancers	Breast, liver, and kidney disorders, ovarian cysts	>100 units per mL	Elevated in about 33% of early-stage breast cancers and about 67% of late-stage breast cancers	1, 2
2	2		Colorectal cancer	Breast, lung, gastric, pancreatic, bladder, medullary thyroid, head and neck, cervical, and hepatic cancers, lymphoma, melanoma	Cigarette smoking, peptic ulcer disease, inflammatory bowel disease, pancreatitis, hypothyroidism, cirrhosis, biliary obstruction	>10 ng per mL	Elevated in less than 25% of early-stage colon cancers and 75% of late-stage colon cancers	3, 4
3	3		Pancreatic cancer, biliary tract cancers	Colon, esophageal, and hepatic cancers	Pancreatitis, biliary disease, cirrhosis	>1,000 units per mL	Elevated in 80% to 90% of pancreatic cancers and 60% to 70% of biliary tract cancers (Note: The greatest possible sensitivity is 95 percent, given that 5% of the population have Lewis-null blood type and are unable to produce the antigen.)	5
4	4		Hepatocellular carcinoma, nonseminomatous germ cell tumors	Gastric, biliary, and pancreatic cancers	Cirrhosis, viral hepatitis, pregnancy	>500 ng per mL	Elevated in 80% of hepatocellular carcinomas; AFP or b-hCG elevated in 85% of nonseminomatous germ cell tumors; elevated in only 20% of early-stage nonseminomatous germ cell tumors	6
5	5		Nonseminomatous germ cell tumors, gestational trophoblastic disease	Rarely, gastrointestinal cancers	Hypogonadal states, marijuana use	>30 mIU per mL	AFP or b-hCG elevated in 85% of nonseminomatous germ cell tumors; elevated in only 20% of early-stage nonseminomatous germ cell tumors	7, 8

Marker_Conditions

6	6		Ovarian cancer	Endometrial, fallopian tube, breast, lung, esophageal, gastric, hepatic, and pancreatic cancers	Menstruation, pregnancy, fibroids, ovarian cysts, pelvic inflammation, cirrhosis, ascites, pleural and pericardial effusions, endometriosis	>200 units per mL	Elevated in about 85% of ovarian cancers; elevated in only 50% of early-stage ovarian cancers	9, 10, 11
7	7		Prostate cancer	None	Prostatitis, benign prostatic hypertrophy, prostatic trauma, after ejaculation	>10 ng per mL	Elevated in more than 75% of organ-confined prostate cancers	12, 13, 14

Marker_Conditions_Ref

Marker_Conditions_Reference Record No	Conditions Record No	Literature_Reference Record No
1	1	1
2	1	2
3	2	3
4	2	4
5	3	5
6	4	6
7	5	7
8	5	8
9	6	9
10	6	10
11	6	11
12	7	12
13	7	13
14	7	14

Marker_Use

Use Record No	Marker_Literature Record No	Screening	Diagnosis	Follow-up after primary treatment	Monitoring of treatment response	Use Reference
1	1	No	No	Consider in patients at high risk for recurrence; obtain CA 27.29 level every 4 to 6 months.	Helpful	1
2	2	No	No	In patients at high risk for recurrence, obtain CEA level every 2 to 3 months for at least 2 years.	Very helpful	16
3	3	No	Selected pancreatic masses	No	Helpful	5

Marker_Use						
4	4	No (Except in highly selected patients with nonalcoholic-induced cirrhosis)	Poorly differentiated cancer of unknown primary; patients with cirrhosis and a liver mass	In patients treated for nonseminomatous germ cell tumor, obtain AFP and b-hCG levels every 1 to 2 months for 1 year, then quarterly for 1 year, and less frequently thereafter.	Essential in patients treated for nonseminomatous germ cell tumor; very helpful in patients treated for hepatocellular carcinoma	8, 20, 41
5	5	No	Poorly differentiated cancer of unknown primary; gestational trophoblastic disease	In patients treated for nonseminomatous germ cell tumor, obtain AFP and b-hCG levels every 1 to 2 months for 1 year, then quarterly for 1 year, and less frequently thereafter. In patients treated for gestational trophoblastic disease, obtain b-hCG level once a month for 6 to 12 months.	Essential in patients treated for nonseminomatous germ cell tumor or gestational trophoblastic disease	8, 24, 41
6	6	No (Except in heritable ovarian cancer syndromes)	Adjunct for diagnosis of pelvic mass in postmenopausal women; malignant ascites in women with cancer of unknown primary	Obtain CA 125 level every 3 months for 2 years, then less frequently.	Very helpful	26, 27, 41
7	7	Yes	Adenocarcinoma of unknown primary; widely positive bone scan and prostate mass	Obtain PSA level every 6 months for 5 years, then annually.39Any detectable PSA after radical prostatectomy indicates recurrence.Three consecutive PSA elevations after radiation therapy indicate recurrence.	Very helpful	12, 39, 40, 41

Marker_Use_Ref		
Marker_Use_Reference Record No	Use Record No	Literature_Reference Record No
1	1	1
2	2	16
3	3	5
4	4	8
5	4	20
6	4	41
7	5	8
8	5	24
9	5	41
10	6	26
11	6	27
12	6	41

Marker_Use_Ref		
13	7	12
14	7	39
15	7	40
16	7	41

Literature_Reference

Literature_Reference Record No	Literature Record No	Reference No	Reference
1	1	1	Chan DW, Beveridge RA, Muss H, Fritsche HA, Hortobagyi G, Theriault R, et al. Use of Truquant BR radioimmunoassay for early detection of breast cancer recurrence in patients with stage II and stage III disease. J Clin Oncol 1997;15:2322-8.
2	1	2	Gion M, Mione R, Leon AE, Dittadi R. Comparison of the diagnostic accuracy of CA27.29 and CA15.3 in primary breast cancer. Clin Chem 1999;45:630-7.
3	1	3	Fletcher RH. Carcinoembryonic antigen. Ann Intern Med 1996; 104:66-73.
4	1	4	Clinical practice guidelines for the use of tumor markers in breast and colorectal cancer. Adopted on May 17, 1996, by the American Society of Clinical Oncology. J Clin Oncol 1996;14:2843-77.
5	1	5	Steinberg W. The clinical utility of the CA 19-9 tumor-associated antigen. Am J Gastroenterol 1990;85:350-5.
6	1	6	Johnson PJ. The role of serum alpha-fetoprotein estimation in the diagnosis and management of hepatocellular carcinoma. Clin Liver Dis 2001;5:145-59.
7	1	7	Fowler JE Jr, Platoff GE, Kubrock CA, Stutzman RE. Commercial radioimmunoassay for beta subunit of human chorionic gonadotropin: falsely positive determinations due to elevated serum luteinizing hormone. Cancer 1982;49:136-9.
8	1	8	Bosl GJ, Bajorin DF, Sheinfeld J, Motzer RJ, Chaganti RS. Cancer of the testis. In: DeVita VT, Hellman S, Rosenberg SA, et al., eds. Cancer, principles and practice of oncology. 6th ed. Philadelphia: Lippincott, Williams & Wilkins, 2001:1491-518.
9	1	9	Tuxen MK, Soletormos G, Dombernowsky P. Tumor markers in the management of patients with ovarian cancer. Cancer Treat Rev 1995;21:215-45.
10	1	10	Gallup DG, Talledo E. Management of the adnexal mass in the 1990s. South Med J 1997;90:972-81.
11	1	11	Chen DX, Schwartz PE, Li XG, Yang Z. Evaluation of CA 125 levels in differentiating malignant from benign tumors in patients with pelvic masses. Obstet Gynecol 1988;72:23-7.
12	1	12	Prostate-specific antigen (PSA) best practice policy. American Urological Association (AUA). Oncology [Huntingt] 2000;14:267-72,277-8,280 passim.
13	1	13	Tchetgen MB, Oesterling JE. The effect of prostatitis, urinary retention, ejaculation, and ambulation on the serum prostate-specific antigen concentration. Urol Clin North Am 1997;24:283-91.
14	1	14	Catalona WJ, Richie JP, Ahmann FR, Hudson MA, Scardino PF, Flanigan RC, et al. Comparison of digital rectal examination and serum prostate specific antigen in the early detection of prostate cancer: results of a multicenter clinical trial of 6,630 men. J Urol 1994;151:1283-90.
15	1	15	Ballesta AM, Molina R, Filella X, Jo J, Gimenez N. Carcinoembryonic antigen in staging and follow-up of patients with solid tumors. Tumour Biol 1995;16:32-41.
16	1	16	Bast RC Jr, Ravdin P, Hayes DF, Bates S, Fritsche H Jr, Jessup JM, et al. 2000 update of recommendations for the use of tumor markers in breast and colorectal cancer: clinical practice guidelines of the American Society of Clinical Oncology. J Clin Oncol 2001;19:1865-78.

Literature_Reference			
17	1	17	Bruinvels DJ, Stiggelbout AM, Kievit J, van Houwelingen HC, Habbema JD, van de Velde CJ. Follow-up of patients with colorectal cancer. A meta-analysis. Ann Surg 1994;219:174-82.
18	1	18	Kim HJ, Kim MH, Myung SJ, Lim BC, Park ET, Yoo KS, et al. A new strategy for the application of CA19-9 in the differentiation of pancreaticobiliary cancer: analysis using a receiver operating characteristic curve. Am J Gastroenterol 1999;94:1941-6.
19	1	19	Tang ZY, Yu YQ, Zhou XD, Yang BH, Ma ZC, Lin ZY. Subclinical hepatocellular carcinoma: an analysis of 391 patients. J Surg Oncol Suppl 1993;3:55-8.
20	1	20	Yuen MF, Cheng CC, Lauder IJ, Lam SK, Ooi CG, Lai CL. Early detection of hepatocellular carcinoma increases the chance of treatment: Hong Kong experience. Hepatology 2000;31:330-5.
21	1	21	International Germ Cell Consensus Classification: a prognostic factor-based staging system for metastatic germ cell cancers. International Germ Cell Cancer Collaborative Group. J Clin Oncol 1997;15:594-603.
22	1	22	Mazumdar M, Bajorin DF, Bacik J, Higgins G, Motzer RJ, Bosl GJ. Predicting outcome to chemotherapy in patients with germ cell tumors: the value of the rate of decline of human chorionic gonadotropin and alpha-fetoprotein during therapy. J Clin Oncol 2001;19:2534-41.
23	1	23	Einhorn LH. Treatment of testicular cancer: a new and improved model. J Clin Oncol 1990;8:1777-81.
24	1	24	Diseases and abnormalities of the placenta. In: Cunningham FG, et al., eds. Williams Obstetrics. 21st ed. New York: McGraw-Hill, 2001:835-47.
25	1	25	Jacobs IJ, Skates SJ, MacDonald N, Menon U, Rosenthal AN, Davies AP, et al. Screening for ovarian cancer: a pilot randomised controlled trial. Lancet 1999;353:1207-10.
26	1	26	National Institutes of Health Consensus Development Conference Statement. Ovarian cancer: screening, treatment, and follow-up. Gynecol Oncol 1994;55(3 pt 2):S4-14.
27	1	27	Malkasian GD Jr, Knapp RC, Lavin PT, Zurawski VR Jr, Podratz KC, Stanhope CR, et al. Preoperative evaluation of serum CA 125 levels in premenopausal and postmenopausal patients with pelvic masses: discrimination of benign from malignant disease. Am J Obstet Gynecol 1988;159:341-6.
28	1	28	Bridgewater JA, Nelstrop AE, Rustin GJ, Gore ME, McGuire WP, Hoskins WJ. Comparison of standard and CA-125 response criteria in patients with epithelial ovarian cancer treated with platinum or paclitaxel. J Clin Oncol 1999;17:501-8.
29	1	29	Crawford ED, Schutz MJ, Clejan S, Drago J, Resnick MI, Chodak GW, et al. The effect of digital rectal examination on prostate-specific antigen levels. JAMA 1992;267:2227-8.
30	1	30	Guess HA, Gormley GJ, Stoner E, Oesterling JE. The effect of finasteride on prostate specific antigen: review of available data. J Urol 1996;155:3-9.
31	1	31	Carter HB, Pearson JD, Metter EJ, Brant LJ, Chan DW, Andres R, et al. Longitudinal evaluation of prostate-specific antigen levels in men with and without prostate disease. JAMA 1992;267:2215-20.
32	1	32	Catalona WJ, Partin AW, Slawin KM, Brawer MK, Flanigan RC, Patel A, et al. Use of the percentage of free prostate-specific antigen to enhance differentiation of prostate cancer from benign prostatic disease: a prospective multicenter clinical trial. JAMA 1998;279:1542-7.
33	1	33	Partin AW, Kattan MW, Subong EN, Walsh PC, Wojno KJ, Oesterling JE, et al. Combination of prostate-specific antigen, clinical stage, and Gleason score to predict pathological stage of localized prostate cancer. A multi-institutional update. JAMA 1997;277: 1445-51.
34	1	34	Catalona WJ, Smith DS, Ratliff TL, Basler JW. Detection of organ-confined prostate cancer is increased through prostate-specific antigen-based screening. JAMA 1993;270:948-54.

Literature_Reference			
35	1	35	Harris R, Lohr KN. Screening for prostate cancer: an update of the evidence for the U.S. Preventive Services Task Force. Ann Intern Med 2002;137:917-29.
36	1	36	Albertsen PC. The role of PSA screening in early detection of prostate cancer. PPO Updates 2001;15:1-16.
37	1	37	Burack RC, Wood DP Jr. Screening for prostate cancer. The challenge of promoting informed decision making in the absence of definitive evidence of effectiveness. Med Clin North Am 1999;83:1423-42, vi.
38	1	38	Oesterling JE, Martin SK, Bergstralh EJ, Lowe FC. The use of prostate-specific antigen in staging patients with newly diagnosed prostate cancer. JAMA 1993;269:57-60.
39	1	39	Millikan R, Logothetis C. Update of the NCCN guidelines for treatment of prostate cancer. Oncology [Huntingt] 1997;11(11A): 180-93.
40	1	40	Pound CR, Partin AW, Eisenberger MA, Chan DW, Pearson JD, Walsh PC. Natural history of progression after PSA elevation following radical prostatectomy. JAMA 1999;281:1591-7.
41	1	41	Greco FA, Hainsworth JD. Cancer of unknown primary site. In: DeVita VT Jr, Hellman S, Rosenberg SA, et al., eds. Cancer, principles and practice of oncology. 6th ed. Philadelphia: Lippincott Williams & Wilkins, 2001:2537-60.

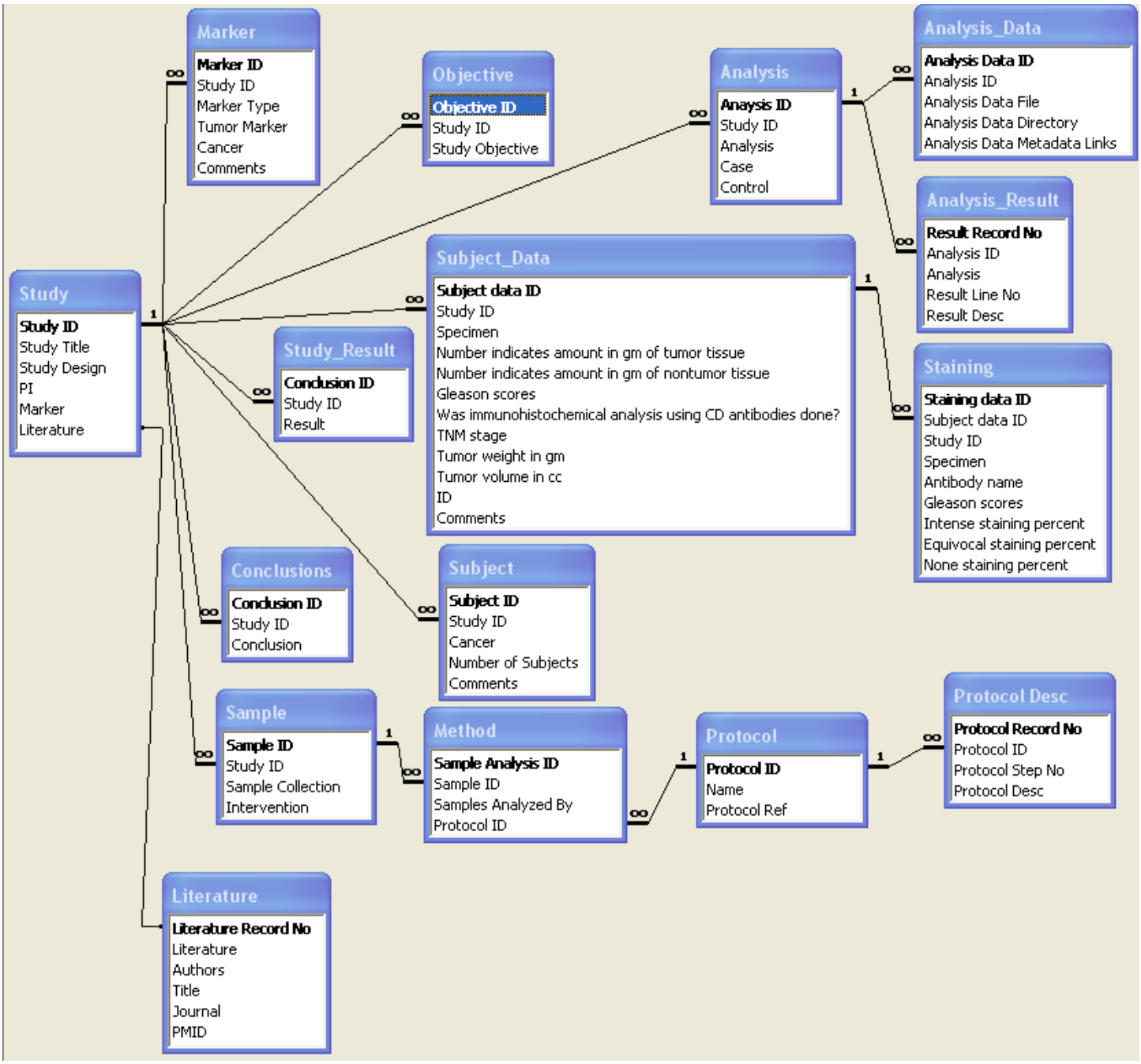
3.3 Query

Marker Query

Marker	Type	Primary tumor	Sensitivity	% elevated tumor marker levels in early stage cancers	% elevated tumor marker levels in late stage cancers
CA 27.29	Serum	Breast cancer	Elevated in about 33% of early-stage breast cancers and about 67% of late-stage breast cancers	33	67
CEA	Serum	Colorectal cancer	Elevated in less than 25% of early-stage colon cancers and 75% of late-stage colon cancers	25	75
CA 19-9	Serum	Pancreatic cancer	Elevated in 80% to 90% of pancreatic cancers and 60% to 70% of biliary tract cancers (Note: The greatest possible sensitivity is 95 percent, given that 5% of the population have Lewis-null blood type and are unable to produce the antigen.)	80	90
CA 19-9	Serum	Biliary tract cancer	Elevated in 80% of hepatocellular carcinomas; AFP or b-hCG elevated in 85% of nonseminomatous germ cell tumors; elevated in only 20% of early-stage nonseminomatous germ cell tumors	60	70

4. Biomarker data populated from “technology” type publications

4.1 Data Model



4.2 Data

Study					
Study ID	**Study Title**	**Study Design**	**PI**	**Marker**	**Literature**
1	Analysis of prostate cancer by proteomics using tissue specimens	Differential analysis of secreted proteins between cancer and non-cancer.	Alvin Y. Liu	TIMP1	1

Literature

Literature Record No	Literature	Authors	Title	Journal	PMID
1	Liu AY, Zhang H, Sorensen CM, Diamond DL. Analysis of prostate cancer by proteomics using tissue specimens. J Urol. 2005 Jan;173(1): 73-8. Erratum in: J Urol. 2005 Mar; 173(3):1051.	Liu AY, Zhang H, Sorensen CM, Diamond DL.	Analysis of prostate cancer by proteomics using tissue specimens.	J Urol. 2005 Jan;173(1): 73-8. Erratum in: J Urol. 2005 Mar;173(3):1051.	15592032

Objective

Objective ID	Study ID	Study Objective
1	1	Use ProteinChip Array SELDI-TOF-MS to profile prostate tissue samples to generate phenomic fingerprints.
2	1	Use quantitative proteomics based on glycopeptide capture followed by tandam MS to identify expressed proteins.

Marker

Marker ID	Study ID	Marker Type	Tumor Marker	Cancer	Comments
1	1	Prostate tissue	Metalloproteinase inhibitor-1 (TIMP1)	Prostate cancer	
2	1	Prostate tissue	PSA		Protein detected by MS in prostate tissue preparations
3	1	Prostate tissue	Prostatic acid phosphatase		Protein detected by MS in prostate tissue preparations
4	1	Prostate tissue	Igγ-2C		Protein detected by MS in prostate tissue preparations
5	1	Prostate tissue	Lumican		Protein detected by MS in prostate tissue preparations
6	1	Prostate tissue	Serum amyloid A-4		Protein detected by MS in prostate tissue preparations
7	1	Prostate tissue	α1-Antitrypsin		Protein detected by MS in prostate tissue preparations
8	1	Prostate tissue	Plasma protease C1 inhibitor		Protein detected by MS in prostate tissue preparations
9	1	Prostate tissue	Complement C3		Protein detected by MS in prostate tissue preparations
10	1	Prostate tissue	α2-Macroglobulin		Protein detected by MS in prostate tissue preparations
11	1	Prostate tissue	Haptoglobins		Protein detected by MS in prostate tissue preparations
12	1	Prostate tissue	AMBP		Protein detected by MS in prostate tissue preparations
13	1	Prostate tissue	α1-Antichymotrypsin		Protein detected by MS in prostate tissue preparations
14	1	Prostate tissue	carboxypeptidase N chain		Protein detected by MS in prostate tissue preparations
15	1	Prostate tissue	α1-Acid glycoprotein		Protein detected by MS in prostate tissue preparations
16	1	Prostate tissue	Complement C4		Protein detected by MS in prostate tissue preparations
17	1	Prostate tissue	Apolipoprotein B-100		Protein detected by MS in prostate tissue preparations
18	1	Prostate tissue	Kininogen		Protein detected by MS in prostate tissue preparations
19	1	Prostate tissue	Inter-α-trypsin inhibitor H4		Protein detected by MS in prostate tissue preparations
20	1	Prostate tissue	Complement C1q subcomponent		Protein detected by MS in prostate tissue preparations

Marker

21	1	Prostate tissue	Peptidoglycan recognition protein L		Protein detected by MS in prostate tissue preparations
22	1	Prostate tissue	Membraine copper amine oxidase		Protein detected by MS in prostate tissue preparations
23	1	Prostate tissue	Microfibril-associated blycoprotein 4		Protein detected by MS in prostate tissue preparations
24	1	Prostate tissue	Collagen α1		Protein detected by MS in prostate tissue preparations
25	1	Prostate tissue	Laminin γ1		Protein detected by MS in prostate tissue preparations
26	1	Prostate tissue	Acid ceramidiase		Protein detected by MS in prostate tissue preparations

Sample

Sample ID	Study ID	Sample Collection	Intervention
1	1	Patient matched cancer and noncancer specimens were digested by collagenase to single cells.	After digestion the cells were pelleted and the cell-free supernatant was used for analysis. A reversed phase hypdrophobic ProteinChip Array was used to generated SELDI patterns.

Method

Sample Analysis ID	Sample ID	Samples Analyzed By	Protocol ID
1	1	Tissue specimen processing	1
2	1	SELDI-TOF-MS proteomics	2
3	1	Glycopeptide capture and quantitative proteomics	3
4	1	Western blotting	4
5	1	Immunohistochemistry	5

Protocol

Protocol ID	Name	Protocol Ref
1	Tissue specimen processing	
2	SELDI-TOF-MS proteomics	
3	Glycopeptide capture and quantitative proteomics	
4	Western blotting	
5	Immunohistochemistry	

Protocol Desc

Protocol Record No	Protocol ID	Protocol Step No	Protocol Desc
1	1	1	Prostate tissue specimens were obtained from resected glands under an institutional review board approved protocol.
2	1	2	The histological composition of the samples was assessed by examining adjacent sections.
3	1	3	Tumor samples were dissected and only tissue that was superfluous to that required for pathological evaluation was taken.
4	1	4	Tissue specimen (in numerical codes) weighing at least 0.1 gm were minced in Hanks' balanced salt solution.
5	1	5	The tissue pieces were placed in RPMI1640 medium supplemented with 5% volume per volume fetal bovine serum and 10-8 M dihydrotestosterone.

Protocol Desc			
6	1	6	Collagenase type I (Gibco BRL, Rockville, Maryland) was added.
7	1	7	The cell suspension was diluted with an equal volume of Hanks' balanced salt solution and centrifuged.
8	1	8	The cell-free supernatant, labeled COL, was stored frozen at -20C.
9	1	9	A silver stained gel showed minimal protein degradation (data not shown, fig. 4).
10	1	10	A lymph node metastasis was similarly processed.
11	1	11	For quantitative proteomic analysis the COL of 1 specimen was prepared with serum-free medium.
12	2	1	COL (1 µl or 1 µl 1/10 diluted in 5 mM HEPES, pH 7.4, and 0.01% Triton X100) was applied to reversed phase H4 (hydrophobic) ProteinChip Arrays prewetted with acetonitrile (ACN).
13	2	2	Samples were washed in a gradient of CAN in water (5% or 50% volume per volume) prior to adding the energy absorbing molecule CHCA (α-cyano-4-hydroxycinnamic acid).
14	2	3	CHCA was reconstituted in 500 µl 50% ACM and 0.5% trifluoroacetic acid, and 0.5 µl was added in 2 applications.
15	2	4	The arrays were then inserted into the ProteinChip Reader (Ciphergen Biosystems), a TOF mass pectrometer.
16	2	5	Analyzed data were collected by an automated protocol and interpreted by ProteinChip Software, version 2.1b (Cyphergen Biosystems).
17	2	6	We chose to focus on peptide species in the mass range of approximately 1,000 to 20,000 Da and, hence, the choice of CHCA.
18	3	1	COL samples (approximately 100 µg proteins) were placed in a coupling buffer of 100 mM Na acetate and 150 mM NaCl, pH 5.5, with 15 mM Na periodate.
19	3	2	Periodate was removed by a desalting Econo-Pac 10DG column (Bio Rad Laboratories, Hercules, CA).
20	3	3	Hydrazide resin (Bio Rad Laboratories) (100 µl) equilibrated in coupling buffer was added.
21	3	4	After coupling the mixture was centrifuged and washed in 8 M urea, 0.4 M NH_4HCO_3.
22	3	5	The protein-resin mixture was heated to 55C, followed by washes in urea-bicarbonate.
23	3	6	The urea was removed and the resin was diluted into 300 µl H_2O for trypsin treatment at 1 µg enzyme per 100 µg protein.
24	3	7	The resin was washed extensively in 1.5 M NaCl, 80% CAN/0.1% trifluoroacetic acid and 100% methanol, and lastly in 0.1 M 0.4 M NH_4HCO_3.
25	3	8	For isotope labeling with succinic anhydride, including specimens of patient matched noncancer (NP) by light d0 (hydrogen) and cancer (CP) by heavy d4 (deuterium), coupled glycopeptides were washed 3 times in dimethylform-amide/pyridine/ H_2O (50%/10%/40%)
26	3	9	Succinic anhydride was added to a final concentration of 2 mg/ml.
27	3	10	After the reaction washes in dimethylform-amide, H_2O and 0.1 M NH_4HCO_3 were done and the peptides were released by PNGase F.
28	3	11	Released peptides were resuspended in 0.4% acetic acid for microcapillary liquid chromatography-MS/MS by a Finnigan LCQ ion trap mass spectrometer (Thermo Finnigan, San Jose, CA).
29	4	1	Equal amounts of protein from CP and NP COL samples (specimen 02-169) were resolved on 4% to 15% sodium dodecyl sulfate-polyacrylamide gel and transferred to Hybond-P membranes (Amersham Biosciences, Piscataway, NJ).
30	4	2	The membranes were treated in phosphage buffered saline containing 0.05% Tween 20 and 5% nonfat dry milk, and then probed with antitissue inhibitor of metalloproteinase-1 (TIMP1) (clone 7-6C1, Chemicon, Temecula, CA) at 1:1,000 for 2 hours.
31	4	3	Antizinc-α2-glycoprotein (ZAG) (H-21, Santa Cruz Biotechnology, Santa Cruz, CA) and antiprostate specific antigen (PSA) (A67-B/E3, Santa Cruz Biotechnology) at 1:1,000 were used to assess sample loading.
32	4	4	Subsequently the membranes were incubated with donkey antigoat (1:10,000, Santa Cruz Biotechnology) or sheep antimouse (1:2,500, Amersham Biosciences) horseradish peroxidase conjugated antibodies.

Protocol Desc

33	4	5	An ECL Plus detection kit (Amersham Biosciences) was used to visualize the reaction by chemiluminiscence.
34	5	1	

Subject

Subject ID	Study ID	Cancer	Number of Subjects	Comments
1	1	Primary prostate tumor	43	
2	1	Matched noncancer specimen	26	

Subject_Data

Subject data ID	Study ID	Specimen	Number indicates amount in gm of tumor tissue	Number indicates amount in gm of nontumor tissue	Gleason scores	Was immuno-histochemical analysis using CD antibodies done?	TNM stage	Tissue weight in gm	Tumor volume in cc	ID	Comments
1	1	98-363	0.21	not done	3+3	yes	T2c	43	1.5		
2	1	98-367	0.15	0.44	3+3	yes	T3a	47	1		
3	1	98-353	0.33	0.32	3+3	yes	T2c	33	2.3		
4	1	98-092	1.51	not done	4+5	no	T4b	not available	15		
5	1	99-002	3.1	not done	3+5	yes	T4b	not available	18	CP6	
6	1	98-082	2.46	not done	5+4	no	T4b	45	20		
7	1	97-270	0.51	0.56	3+3	no	T2c	36	3.6		
8	1	99-001	0.6	not done	4+3	no	T3c	35	5.6	CP8	
9	1	98-350	0.81	1.1 BPH	3+3	yes	T2c	32	8.35		
10	1	98-351	0.2	0.82	3+5	no	T2c	33	1.85		
11	1	97-327	0.17	5.62	3+4	no	T3c	68	0.6		
12	1	97-230	0.57	0.98	4+3	no	T2c	35	4		
13	1	97-242	0.66	0.4	4+3	no	T3a	37	6		
14	1	98-352	0.31	0.82	3+5	yes	T3a	50	3.95		
15	1	97-222	2.1	not done	4+3	yes	T2c	42	5.5		
16	1	98-335lg	0.37	not done	3+4	no	T3b	65	8		tumor of large gland; Tumor of large and small glands were dissected from same prostatethey showed similar SELDI pattern.

Subject_Data											
17	1	98-335sm	0.5								tumor of small gland; Tumor of large and small glands were dissected from same prostatethey showed similar SELDI pattern.
18	1	98-095	nd	4.78 BPH	3+3	no	T2c	102	2.1		benigh prostatic hyperplasia (BPH) specimen
19	1	97-231	1.67	1.02	4+4	no	T3c	50	9		
20	1	99-007	0.53	0.71	4+3	yes	T3a	40	9		
21	1	98-389	0.33	0.6	4+3	no	T2cN1	40	4.6		
22	1	98-336	1.18	not done	4+3	yes	T3c	48	>25		
23	1	99-044	0.12	0.11	3+3	no	T2c	54	1	CP3	
24	1	98-366	0.18	not done	3+4	yes	T3aN2	41	6		
25	1	98-346	0.2	1.17 BPH	3+3	yes	T2b	73	1.8		
26	1	97-319	0.31	0.67	3+3	no	T2c	28	1.7		
27	1	97-266	0.43	0.28	4+3	no	T2c	32	3.9		
28	1	97-326	0.43	0.79	4+3	no	T3a	42	3		
29	1	99-010	0.34	0.5	3+3	yes	T2a	37	4	CP4	
30	1	99-004	0.24	0.36	4+3	yes	T2a	37	2.7	CP7	
31	1	98-345	0.18	2 BPH	3+2	yes	T2a	45	0.9		
32	1	98-009	0.84	not done	3+4	yes	T3a	31	4.5		
33	1	98-091	0.29	0.54	3+4	no	T3a	57	6		
34	1	98-365	nd	0.4 BPH	3+3	no	T2a	79	4.2		benigh prostatic hyperplasia (BPH) specimen
35	1	98-094	0.44	not done	3+4	yes	T2c	57.7	4.5		
36	1	98-381	0.35	0.54	3+4	yes	T3cN1	70	9.5		
37	1	98-348	0.68	not done	4+5	yes	T4N1	not available	19		
38	1	98-104	0.39	not done	3+3	yes	T2c	47	2		
39	1	97-264	1.1	0.32	3+4	no	T3a	47	7.3		
40	1	98-107	0.57	0.29	3+3	yes	T3c	49	5.2		
41	1	98-089	0.6	not done	3+4	no	T3c	52	6		
42	1	98-088	0.47	not done	3+4	no	T2c	63.5	3.8		
43	1	98-370	0.47	0.63	3+3	no	T2c	39	4.4		

Subject_Data

44	1	99-042	1.93	not done	4+5	no	T4N1	not available	>40	CP5	corresponding prostate tumor specimen of lymph node containing cancer metastasis
45	1	99-042LN	1								lymph node containing cancer metastasis
46	1	98-106	1.03	not done	4+3	yes	T2c	not available	8		
47	1	98-398	0.21	0.42	3+4	yes	T2c	41	2		

Staining

Staining data ID	Subject data ID	Study ID	Specimen	Antibody name	Gleason scores	Intense staining percent	Equivocal staining percent	None staining percent
1	1	1	98-363	CD10	3+3	0	0	100
2	2	1	98-367	CD10	3+3	0	0	100
3	3	1	98-353	CD10	3+3	0	0	100
4	5	1	99-002	CD10	3+5	0	0	100
5	9	1	98-350	CD10	3+3	95	5	0
6	14	1	98-352	CD10	3+5	0	0	100
7	15	1	97-222	CD10	4+3	0	50	50
8	20	1	99-007	CD10	4+3	0	50	50
9	22	1	98-336	CD10	4+3	0	0	100
10	24	1	98-366	CD10	3+4	0	0	100
11	25	1	98-346	CD10	3+3	0	0	100
12	29	1	99-010	CD10	3+3	0	0	100
13	30	1	99-004	CD10	4+3	0	0	100
14	31	1	98-345	CD10	3+2	0	0	100
15	32	1	98-009	CD10	3+4	0	0	100
16	35	1	98-094	CD10	3+4	0	0	100
17	36	1	98-381	CD10	3+4	70	30	0
18	37	1	98-348	CD10	4+5	10	0	90
19	38	1	98-104	CD10	3+3	95	5	0
20	40	1	98-107	CD10	3+3	0	0	100
21	46	1	98-106	CD10	4+3	0	0	100
22	47	1	98-398	CD10	3+4	0	0	100

Study_Result

Conclusion ID	Study ID	Result
1	1	SELDI profiles showed that cancers of similar TNM stages were more likely to have similar profiles.
2	1	On quantitative proteomics tissue metalloproteinase inhibitor-1 (TIMP1) was identified to be down-regularted in cancer.

Study_Result

3	1	Tissue TIMP1 expression was localized to secretory cells.

Conclusion

Conclusion ID	Study ID	Conclusion
1	1	Protein profiling by SELDI is relatively easy to perform and it has great potential in prostate cancer diagnosis through pattern recognition.
2	1	Quantitative proteomics can potentially determine the identity of many biomarkers specific for prostate cancer.

Analysis

Anaysis ID	Study ID	Analysis	Case	Control
1	1	Reproducibility of protein profiling by SELDI-TOF-MS	Prostate tumor tissue/ cells	Prostate noncancer tissue/ cells
2	1	Cancer phenomic fingerprints	Prostate tumor tissue/ cells	Prostate noncancer tissue/ cells
3	1	Down-regulation of TIMP1 expression in prostate cancer	Prostate tumor tissue/ cells	Prostate noncancer tissue/ cells

Analysis_Result

Result Record No	Analysis ID	Analysis	Result Line No	Result Desc
1	1	Reproducibility of protein profiling by SELDI-TOF-MS	1	Five replicates of paired CP and NP (specimen 99-044) were screened on 2 H4 arrays.
2	1	Reproducibility of protein profiling by SELDI-TOF-MS	2	Protein profiles generated from the replicates were virtually identical with regard to the peaks detected and the relative ion intensity, which demonstrated reproducibility for rapid analysis of small volumes of proteins of prostate tumor tissues.
3	1	Reproducibility of protein profiling by SELDI-TOF-MS	3	One peptide species appeared to be associated with CP, while another appeared to be restricted to NP.
4	2	Cancer phenomic fingerprints	1	A large number of samples were then profiled.
5	2	Cancer phenomic fingerprints	2	After the individual patterns were displayed groupings of similar patterns were attempted by visual inspection.
6	2	Cancer phenomic fingerprints	3	As defined by CD phenotypes, the cancer cell type composition was similar for CP3, CP4 and CP7, whereas it was more heterogeneous for CP6 and CP8 (data not shown).
7	3	Down-regulation of TIMP1 expression in prostate cancer	1	The glycopeptide capture method was used to select secreted proteins in specimen 02-167 for MS/MS identification.
8	3	Down-regulation of TIMP1 expression in prostate cancer	2	The collision induced dissociation spectra generated for the peptide species were searched against the National Cancer Institute database using SEQUEST and the identified proteins were quantified using the stable isotope quantification software ASAPratio.
9	3	Down-regulation of TIMP1 expression in prostate cancer	3	The result showed that almost all identified proteins were known to be secreted and the more abundant prostatic proteins of PSA and prostatic acid phosphatase were found (see Appendix)
10	3	Down-regulation of TIMP1 expression in prostate cancer	4	The protein with the highest statistical score for differential expression was TIMP1.
11	3	Down-regulation of TIMP1 expression in prostate cancer	5	The level of 1 identifier TIMP1 peptide in CP was only 0.255-fold of that in NP.

Analysis_Result

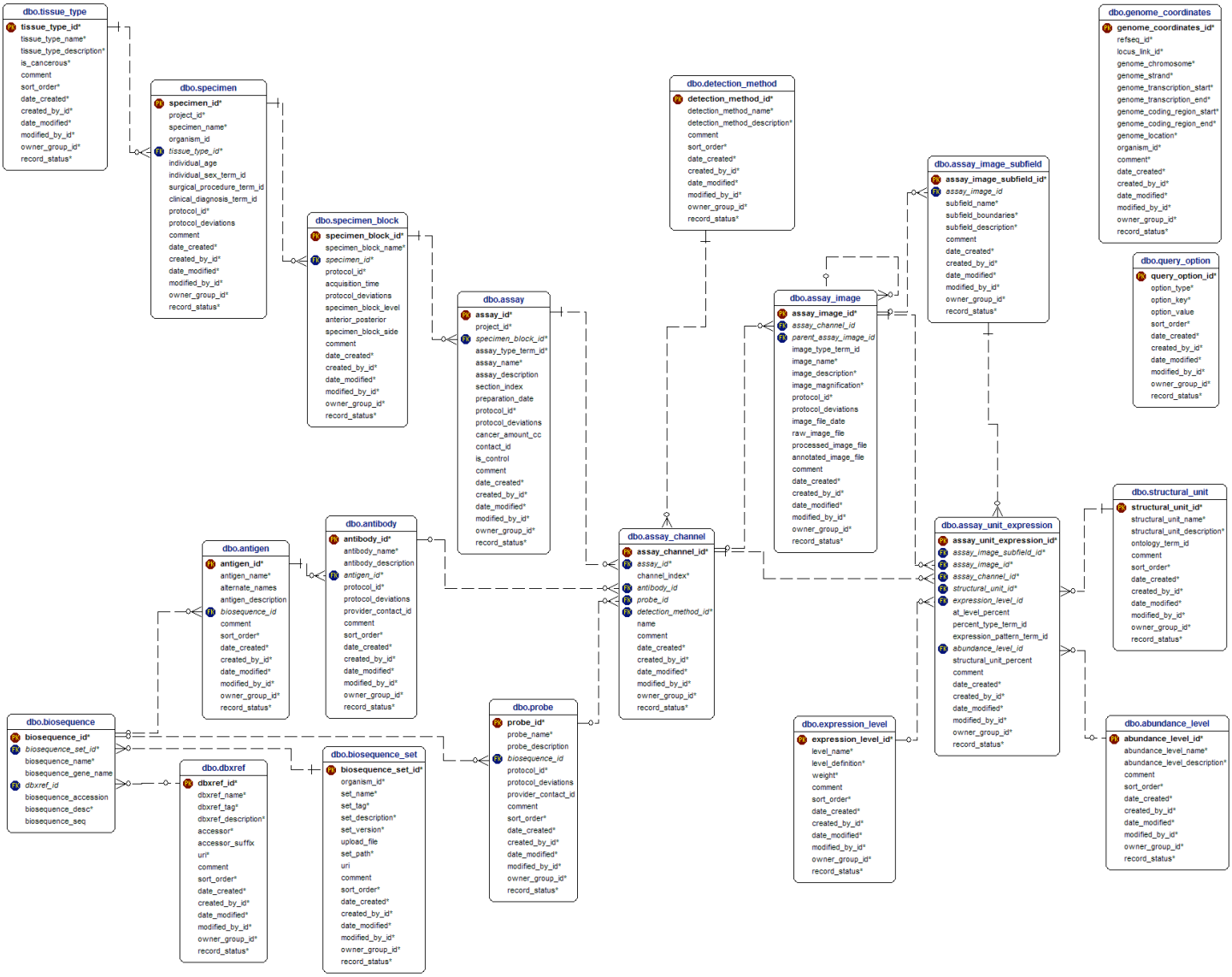
12	3	Down-regulation of TIMP1 expression in prostate cancer	6	Differential TIMP1 expression was verified by Western blot.
13	3	Down-regulation of TIMP1 expression in prostate cancer	7	The amount of detectable TIMP1 in CP was less than that in NP.
14	3	Down-regulation of TIMP1 expression in prostate cancer	8	As the control ZAG and PSA were not differentially expressed.
15	3	Down-regulation of TIMP1 expression in prostate cancer	9	Immunohistochemistry in 15 specimens containing cancer was done and the staining result showed that TIMP1 was localized to the luminal cells of benign glands of specimen 99-022H.
16	3	Down-regulation of TIMP1 expression in prostate cancer	10	Western blotting was also done in 6 more matched NP and CP COLs and in every case a decrease in TIMP1 was seen in CP.

Analysis_Data

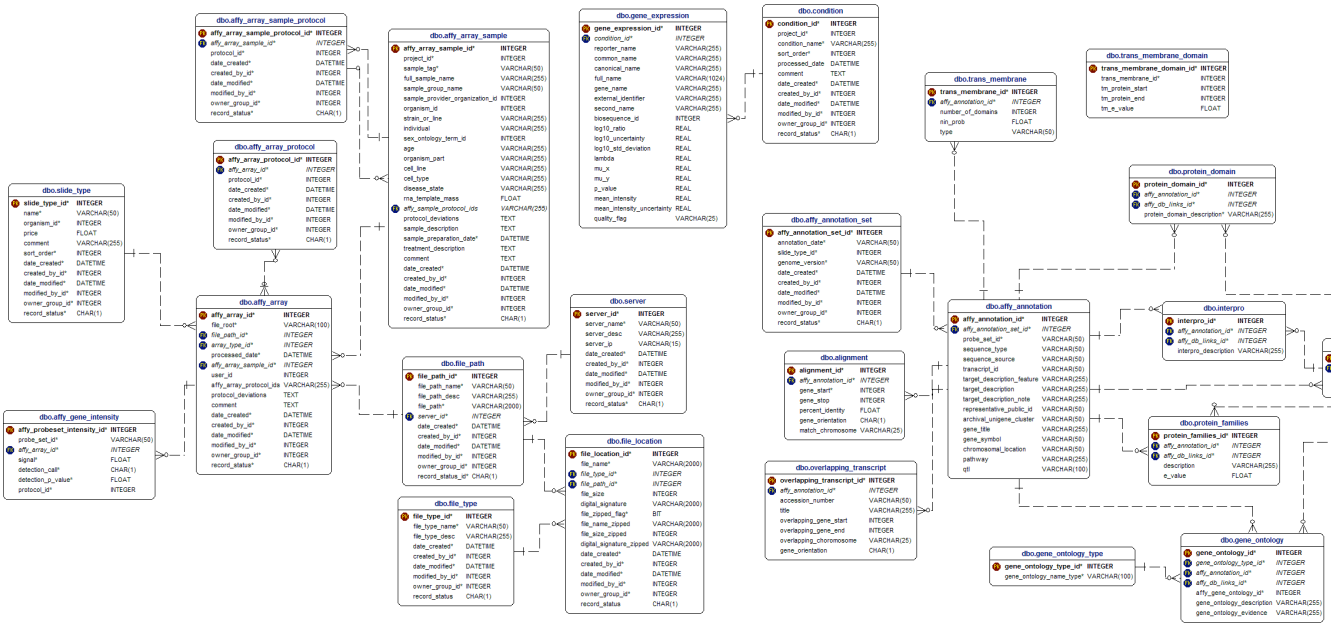
Analysis Data ID	Analysis ID	Analysis Data File	Analysis Data Directory	Analysis Data Metadata Links
1	1	ms_data_1.tar		

4.3 Link to Science Data (eCAS)

4.3.1 “Immunostain.gif” File



4.3.2 “Microarray_Affy_Schema.gif” File



4.3.3 “ms_data_1.tar” File

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